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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,419	08/15/2008	William W. Bachovchin	TUV-048.01	7018

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EXAMINER	
PIHONAK, SARAH	

ART UNIT	PAPER NUMBER
1627	

MAIL DATE	DELIVERY MODE
03/04/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,419	BACHOVCHIN ET AL.	
	Examiner	Art Unit	
	SARAH PIHONAK	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *8-12,15 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 13-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/1/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a national stage entry of PCT/US05/06127, filed on 2/23/2005.

Priority

This application claims priority from Provisional Application No. 60/547226, filed on 2/23/2004.

Response to Restriction Requirement

1. Applicant's election with traverse of the invention of Group I, claims 1-7, 13, and 14, in the reply filed on 12/11/2009 is acknowledged. The traversal is on the ground(s) that it would not constitute an undue burden on the examiner to search all of the claimed inventions. This is not found persuasive because the instant application is a national stage entry of an international application, and unity of invention is a requirement of such applications. In order for different inventions to possess unity of invention, the claimed inventions must be have a special technical feature, which is novel and non-obvious over the prior art. See M.P.E.P. 1850. However, the claimed compounds of Group I do not present a novel contribution over the prior art, as they are disclosed in Scheidt et. al., *Bioorganic and Medicinal Chemistry Letters*, **6**, pp. 2477-2494, (1998). This reference is discussed in below in the rejection under 35 USC § 102(b). Therefore, as the compounds of formula I are not novel, they lack a special technical feature. As there is no special technical feature to link the inventions of Groups I-V, unity of invention is lacking.

The requirement is still deemed proper and is therefore made FINAL.

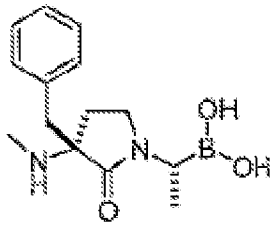
2. Claims 8-9, 10-12, 15, and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/11/2009.

For the species election for a compound of formula I, the Applicants elected compounds G, M, J, and P, as referred to on page 23 of the application.
The elected compounds have been found to be free of the prior art. Therefore, the search was expanded to other compounds of formula I.

3. Claims 1-7, 13, and 14 were examined.

4. Claims 1-7, 13, and 14 are rejected.

5. It is noted that the Applicants have defined the variables L, X, Y, and R^1 as being either absent or present with the claimed substituents. Additionally, in the specification, the Applicants have named exemplary structures of the invention as including the compound shown below (p. 23 of specification):



O

For this compound, the amine group is substituted by methyl. However, Y is not defined as being an alkyl group. The only variable that includes an alkyl group is L or R^1.

Therefore, it has been interpreted by the examiner that if Y or X are absent, the acyclic nitrogen can have a direct bond with either L or R^1.

Claim Rejections-35 USC § 102

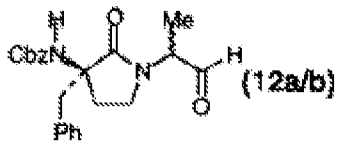
6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

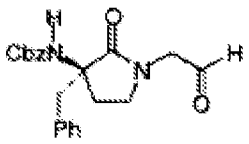
7. Claims 1-2, and 4-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Scheidt et. al., *Bioorganic and Medicinal Chemistry Letters*, **6**, pp. 2477-2494, (1998).

8. The claims are drawn to a compound of formula I, and a pharmaceutical composition comprised of a compound of formula I.

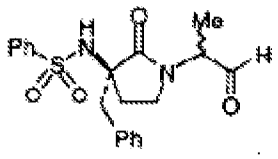
Scheidt et. al. discloses the synthesis and activity of protease inhibitors (Abstract). The compounds disclosed by Scheidt et. al. of formula I are shown below (p. 2482, Table 1, compounds 12a/b, 18, 25, and 29):



(12a/b)



(18)

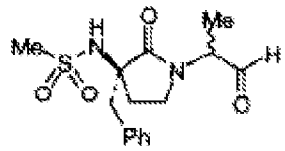


(25)

Where, for 12a/b, Cbz=benzyloxycarbonyl; R^3=CH_2-phenyl; R^2=H; Y=-C(=O); X=O; L=CH_2; R^1=phenyl; n=0; R^4=H; R^5=methyl; R^6=C(=O)R^{12}; R^{12}=H.

For 18, Cbz=benzyloxycarbonyl; R^3=CH_2-phenyl; R^2=H; Y=-C(=O); X=O; L=CH_2; R^1=phenyl; n=0; R^4=H; R^5=H; R^6=C(=O)R^{12}; R^{12}=H.

For 25, Y=SO_2; X=absent; L=absent; R^1=phenyl; R^3=CH_2-phenyl; R^2=H; R^4=H; R^5=methyl; R^6=C(=O)R^{12}; R^{12}=H.



(29)

For compound 29, Y=SO_2; X=absent; L=absent; R^1=methyl; R^3=CH_2-phenyl; R^2=H; R^4=H; R^5=methyl; R^6=C(=O)R^{12}; R^{12}=H.

Scheidt et. al. discloses combining the claimed compounds in a pharmaceutically acceptable solvent, such as DMSO (p. 2491, right column, last sentence-p. 2492, left column, top paragraph). Therefore, as Scheidt et. al. discloses the compounds in a pharmaceutically acceptable solvent, pharmaceutically compositions of the compounds are disclosed. While Scheidt et. al. does not explicitly disclose that the compounds inhibit dipeptidyl peptidase IV with a Ki of 50 nM or less, or are orally active in a mammal, these characteristics are properties of the compounds. A compound and its properties are not patentably distinct from each other, In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). As such, Scheidt et. al. anticipates the claims.

Claim Rejections-35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

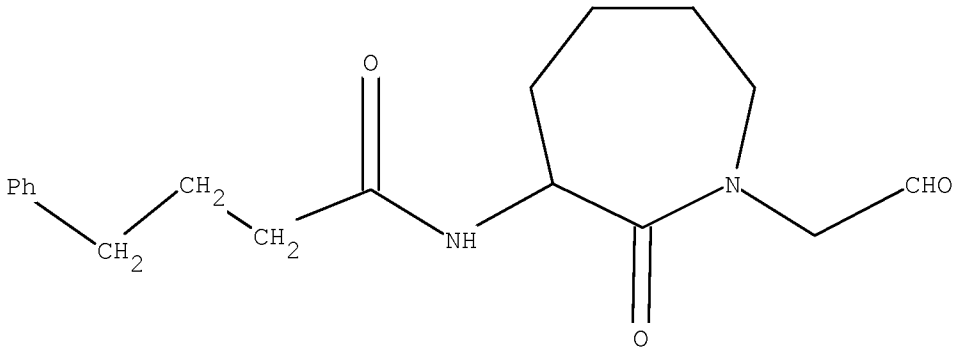
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-2, and 4-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Giannessi et. al., EP Patent No. 462949.

The claims are drawn to a compound of formula I, and a pharmaceutical composition comprised of a compound of formula I.

Giannessi et. al. discloses a compound of formula I as an active pharmaceutical agent, in pharmaceutical compositions, for oral administration (Abstract; p. 2, lines 33-34). The compound disclosed by Giannessi et. al. is shown below (p. 5, example 5, lines 25-51, preparation of compound ST 800):



Where n=2; R^4=H; R^5=H; R^6=C(=O)R^{12}; R^{12}=H; R^3=H; R^2=H; Y=-C(=O); X=absent; L=propyl; R^1=phenyl; R^7=absent; L (from ring structure)=absent. While Giannessi et. al. does not explicitly disclose that the compound is a protease inhibitor, or inhibits dipeptidyl peptidase IV with a Ki of 50 nM or less, these characteristics are properties of the compound. A compound and its properties are not patentably distinct from each other, In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). Therefore, Giannessi et. al. anticipates the claims.

Claim Rejections-35 USC § 102

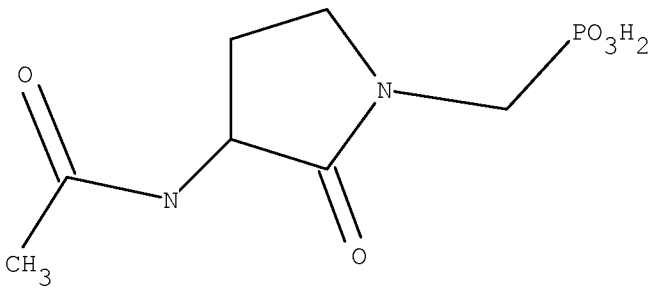
11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-2, and 4-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Natchev, *Synthesis*, **12**, pp. 1079-1084, (1987).

The claims are drawn to a compound of formula I, and a pharmaceutical composition comprised of a compound of formula I.

Natchev discloses a compound of formula I, which is shown below (p. 1082, right column, Scheme C, compound 23; p. 1083, right column, Scheme D, compound 23):



Where n=0; R^4=H; R^5=H; R^6=-P(=R^9)$R^{10}R^{11}$; R^9=O; R^{10}=OLR^{13}; R^{13}=H, and L=absent; R^{11}=OLR^{13}; R^{13}=H, and L=absent; R^2=H; Y=-C(=O); X=absent; L=CH_2; R^1=H. Natchev et. al. also discloses the compound in a pharmaceutically acceptable solvent such as water (p. 1081, Table, compound 23); therefore, the compound is disclosed as being in a pharmaceutical composition. While Natchev et. al. does not explicitly disclose that the

compound is a protease inhibitor, or inhibits dipeptidyl peptidase IV with a Ki of 50 nM or less, these characteristics are properties of the compound. A compound and its properties are not patentably distinct from each other, In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). Therefore, Natchev et. al. anticipates the claims.

Claim Rejections-35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scheidt et. al., *Bioorganic and Medicinal Chemistry Letters*, **6**, pp. 2477-2494, (1998), as applied to claims 1-2, and 4-7 above, and further in view of Remington's: the Science and Practice of Pharmacy, 19th edition, vol. 1, p. 806.

As discussed supra, Scheidt et. al. discloses compounds of formula (I), as well as the compounds in a pharmaceutically acceptable solvent.

Scheidt et. al. does not teach a packaged pharmaceutical, comprising preparation of a compound with instruction describing the use of the preparation.

Remington's teaches that the labeling of pharmaceuticals, along with instructions for preparation of the pharmaceutical for prescription and usage is a requirement by law, under 21 CFR 201.57 (p. 806, left column, 4th full paragraph-right column, all paragraphs). The ability to inhibit a post-proline cleaving enzyme, as well as to regulate glucose metabolism, are properties of the claimed compounds. Therefore, as Remington's teaches that proper labeling and descriptive information of pharmaceuticals, as well as instructions for use are a requirement by law, it would have been prima facie obvious for one of ordinary skill in the art, at the time of the invention, to include information along with the pharmaceutical with instructions for the preparation of inhibiting a post-proline cleaving enzyme, and for regulating glucose metabolism.

Additionally, packaging of the pharmaceutical would have been considered a part of labeling and providing descriptive information and instructions for the drug compounds.

Claim Rejections-35 USC § 112

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 1-7, 13, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a compound of formula I. In the structure, there are two different structural variables which have different points of attachment that are defined as L. While the Applicants have defined what substituents are included as L, it is not certain which L is being referred to, or if one variable defined as L can have the same or a different substituent than the second L variable. As such, the claim is indefinite. Claims 2-7, 13, and 14, which are dependent claims of claim 1, are rejected for the same reason. For prior art purposes, it was interpreted that the two L variables could be defined independently.

Information Disclosure Statement

19. The information disclosure statement (IDS) submitted on 9/1/2009 was filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 8:00 AM - 6:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S.P.

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1627